IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA
AT CLARKSBURG

MERCK SHARP & DOHME CORP., *Plaintiff,* v. **MYLAN PHARMACETICALS, INC.,** *Defendant.*	C.A. No. 1:19-cv-101(IMK)

MYLAN'S OPENING POST-TRIAL BRIEF

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I. INTRODUCTION.

Claims 17 and 20 of Reference Patent 6,699,871 ("the '871 patent") recite sitagliptin or "a pharmaceutically acceptable salt thereof." Despite its express verbiage, and the over fifteen years of protection Merck has enjoyed for its sitagliptin products from those claims (which expire July 26, 2022), Merck tried this case as though the '871 patent is directed to sitagliptin free base alone—casually ignoring the express inclusion of pharmaceutically acceptable salts within the scope of reference claims 17 and 20. But Plaintiff cannot wish away the clear language of the '871 patent to prop up later expiring claims to the exact same thing. The record is clear: the dihydrogenphosphate ("DHP") salt of sitagliptin, as claimed in the asserted 7,326,708 patent ("the '708 patent"), *is* a pharmaceutically acceptable salt of sitagliptin indistinct from the reference claims. That is true based on both the '871 reference patent alone, as well as the prior art in combination with that patent. And, contrary to Merck's argument, Mylan does not need to prove a POSA would *select* the DHP salt of sitagliptin over the free base, or over the HCl salt, or over every other possible salt. Mylan need only show that the '708 claims are not patentably distinct from the reference '871 claims, and that is precisely what was established at trial.

Against this, Merck strained to find purported differences between the reference and asserted claims—the most notable of which is Merck's allegation that the specific 1:1 stoichiometry of phosphate to sitagliptin in sitagliptin DHP somehow differentiates it. The evidence said otherwise. As shown at trial, that stoichiometry was the most reasonably expected for any sitagliptin salt made from phosphoric acid. There was no magic associated with the 1:1 ratio. For these reasons, the asserted claims of the '708 patent are not patentably distinct under the obviousness-type double patenting ("OTDP") doctrine from reference claims 17 and 20 of the prior '871 patent.

There is more. Because the deficiencies with the asserted claims do not end with OTDP. In Merck's zeal to extend its monopoly over sitagliptin compounds, it also claimed far more than the '708 patent disclosure supports. On this, it is remarkable how few facts are in dispute. Merck concedes that it only had a single monohydrate in its possession (claims to which will survive irrespective of the outcome here because those claims were dropped at the eve of trial). Yet Merck pushed for far broader claims—ones that are directed to all hydrates (not just the monohydrate it had) and all other forms that could ever exist—known or unknown. Equity demands that Merck be limited to that which it actually discovered, not more, especially because Merck previously patented sitagliptin itself in the '871 patent. On these facts, the law holds the lack of possession means the asserted patent lacks adequate written description.

Finally, Merck fares no better on enablement. Defending its monohydrate claims from invalidation before the PTAB, Merck vigorously contended that hydrate formation is unpredictable and requires undue experimentation. That fact does not change now that Merck is on the other side of Mylan's IPR challenge. Further, the evidence—most of which is undisputed—established the utter dearth of guidance in the '708 specification, the claims, or anywhere else in the intrinsic record that would enable any hydrate other than the monohydrate. That is not surprising: Merck only possessed one single hydrate. And, while Merck now posits that support for a claim to all hydrates is satisfied by a disclosure of only one hydrate, the law says otherwise. If Merck's theory were to be adopted, it would mean that all one would need to do is add the verbiage, "or hydrates thereof" to a claim and that claim would cover every hydrate—known or unknown; in the past or in the future—of the claimed compound, irrespective of the disclosure. As the Federal Circuit has pronounced, the "*quid pro quo*" of the patent bargain warrants a result where Merck is kept to what it discovered and what it disclosed.

II. OTDP AND THE ASSERTED CLAIMS OF THE '708 PATENT.

A later filed claim is not patentably distinct if it would have been obvious to a POSA in view of the earlier claim alone or in combination with the prior art. *Sun Pharm. Indus., Ltd. v. Eli Lilly & Co.*, 611 F.3d 1381, 1385 (Fed. Cir. 2010); *see Abbvie v. M. & T. Kennedy Inst.*, 764 F.3d 1366, 1374, 1378-79 (Fed. Cir. 2014). The analysis entails two steps: (1) identify the differences between the reference claim of the earlier-expiring patent and the claim of the later-expiring patent; and (2) determine if those differences render the later claim patentably distinct. The second step is analogous to an obviousness analysis. *Id*. But, unlike standard obviousness, in OTDP one *always begins* with the reference claim. *See Sun Pharm.*, 611 F.3d at 1385.[1]

A. Claims 1 and 2 of the '708 Patent Are Not Patentably Distinct.

Reference claim 17 of the '871 patent claims sitagliptin in the (R)-configuration, "or a pharmaceutically acceptable salt thereof." DTX-2054.22 at 41:1-14; Tr. 309:13-18 (Buckton); Tr. 948:20-949:5 (Myerson). Asserted claims 1 and 2 of the '708 patent specifically claim the DHP salt of sitagliptin (claim 2 specifies the (R)-configuration).[2] JTX-1.14 at 15:64-16:30; Tr. 278:17-25, Tr. 280:22-281:1 (Buckton). The question for this Court with respect to claims 1 and 2 is whether (R)-sitagliptin DHP salt is patentably distinct from (R)-sitagliptin "or a pharmaceutically acceptable salt thereof" in reference claim 17 of the '871 patent?

The answer is no. Central to the Court's inquiry is the meaning of "a pharmaceutically acceptable salt" as recited in reference claim 17. To determine the meaning of this term, courts often look to the specification of the reference patent "to learn the meaning of [claim] terms, and

[1] Another distinction is that § 103 obviousness requires inquiry into a motivation to modify the prior art. OTDP does not. *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1378 n.1 (Fed. Cir. 2003). Regardless though, as discussed herein, there was nonetheless a motivation and reasonable expectation of success when it comes to claims 1-3 and 19 of the '708 patent.

[2] Side-by-side comparisons of the reference claims and asserted claims are provided in Exhibit A.

to interpret . . . the coverage of [a] claim." *Sun Pharm.*, 611 F.3d at 1387-88 (quotations omitted). Here, the '871 patent defines "pharmaceutically acceptable salts" as "salts prepared from pharmaceutically acceptable non-toxic bases or acids including . . . inorganic or organic acids." DTX-2054.4 at 6:38-41; Tr. 309:22-310:6 (Buckton). It then goes on to specify only eight "particularly preferred" acids to make the claimed pharmaceutically acceptable salt. One of those preferred acids is phosphoric acid—the precise one used to form the salt claimed in asserted claims 1 and 2. DTX-2054.5 at 7:2-4; Tr. 310:7-13 (Buckton); *see Sun Pharm.*, 611 F.3d at 1387-88. Where the reference claim includes "pharmaceutically acceptable salts," and the reference specification describes such salts as being formed using only eight particularly preferred non-toxic acids (phosphoric acid being one of them), a separate patent with a claim to that precise salt cannot be patentably distinct.[3]

Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348 (Fed. Cir. 2007), is instructive. At issue was a claim directed to "[t]he besylate salt of amlodipine." *Id.* at 1356. Amlodipine besylate is an acid-addition salt formed from reacting amlodipine and benzene sulphonic acid. *Id.* at 1353. The prior art included a patent claiming amlodipine and its pharmaceutically acceptable salts, and it listed several acid-addition salts. *Id.* But—unlike the reference patent here—the prior art in *Pfizer* did *not* reference the specific acid (benzene sulphonic acid) recited in the asserted claims. *Id.* at 1356. Notwithstanding this omission, the Federal Circuit outright *reversed* the district court and held the patent invalid as obvious. *Id.* at 1372.

[3] At trial, Plaintiff's expert Dr. Myerson discussed pKa, solubility, activity, dosage form, dose, and a theory that a POSA would only consider the HCl salt before considering other acids for salt formation. Tr. 860:6-11, 871:7-874:14 (Myerson). Mylan disputes the import and relevance of these "considerations" as discussed herein. But regardless, during cross examination, Dr. Myerson conceded those "considerations" are not mentioned in the definition of "pharmaceutically acceptable salts." Tr. 949:16-950:12 (Myerson).

In light of *Pfizer*, it is arduous to see how the '708 patent can survive OTDP scrutiny. *See Abbvie*, 764 F.3d at 1378 (observing that OTDP "is analogous to an obviousness analysis"). Like *Pfizer*, the reference patent here claims sitagliptin and its pharmaceutically acceptable salts. But it then goes a step further and discloses the *specific acid* used to produce the salt in Merck's asserted claims. And, for good measure, the reference patent also teaches phosphoric acid as "particularly preferred" for making the claimed pharmaceutically acceptable salts. More detail—and especially the call-out of phosphoric acid in the reference specification—means that Mylan has an even stronger invalidity defense than the successful defendant in *Pfizer*.

If that were not enough (and it should be), the Federal Circuit in *Pfizer* outright rejected a number of the exact arguments Merck put forth to undermine an OTDP finding, namely[4]:

- Recognizing (contrary to Merck's position here) the motivation of a POSA to make active drug molecules "into pharmaceutically acceptable acid addition salts to improve their bioavailability." *Id.* at 1353.
- Rejecting the idea that salts would not be obvious just because they were less frequently used in FDA-approved drugs than hydrochloride salts: "That benzene sulphonate was only used in creating 0.25% of FDA-approved drugs is not highly probative, much less dispositive. Indeed, beyond hydrochloride, which was used in approximately 43% of approved drugs, almost all other salts could be characterized as 'rarely used.'" *Id.* at 1363.
- Rejecting the notion that a POSA would not have a reasonable expectation of success in forming a salt just because the properties of each salt must be verified through testing: "Indeed, a rule of law equating unpredictability to patentability, applied in this case, would mean that any new salt — including those specifically listed in the [prior art] patent itself — would be separately patentable, simply because the formation and properties of each salt must be verified through testing. This cannot be the proper standard since the expectation of success need only be reasonable, not absolute." *Id.* at 1364.

[4] Merck's claim that *Pfizer* does not govern – while not surprising – misconstrues the law. And, its reliance on *Valeant* is inapposite. Tr. 27:12-21 (Merck Opening). *Valeant* dealt with the question of whether it would be obvious to change a hydrochloride salt of buproprion to a hydrobromide salt—it did not address whether the hydrobromide salt would have been obvious over an earlier claim to buproprion or "a pharmaceutically acceptable salt thereof". *Valeant Int'l v. Watson Pharms.*, 2011 WL 6792653, at *7 (S.D. Fla. Nov. 8, 2011). The same is true for *Pfizer v. Mylan*, which is even further removed in that the Court disagreed with the defendants' lead compound analysis—an analysis not applicable here because the agreed upon starting point is sitagliptin or a pharmaceutically acceptable salt thereof. *Pfizer Inc. v. Mylan Pharms. Inc.*, 71 F. Supp. 3d 458, 470-71 (D. Del. 2014).

- Noting that the prior art placed no limitations on the choice of salt whatsoever, except that it be non-toxic and formed from an acid containing a pharmaceutically-acceptable anion, and therefore to a POSA there was "a strong suggestion that any and all pharmaceutically acceptable anions would form non-toxic acid addition salts and would work for their intended purpose. . . ." *Id*. at 1365.

Against this backdrop, and as Mylan's expert Dr. Buckton explained, there was a clear motivation and reasonable expectation of success in forming a salt using phosphoric acid given the express definition of "pharmaceutically acceptable salts" in the reference '871 patent.

That leaves Merck to argue that the 1:1 stoichiometry of the DHP salt claimed in the '708 patent somehow makes it patentably distinct from the reference '871 patent. It does not.[5] Witnesses on both sides agreed that a 1:1 DHP would be *the phosphate salt reasonably expected*, even if some other stoichiometry may be possible. Tr. 314:16-315:11 (Buckton); *see* Tr. 159:13-18, 162:6-9, 162:22-163:1, 163:8-11, 163:19-22 (Hansen); 724:5-725:11, 726:4-23 (Vydra). But a mere possibility cannot trump what is actually expected. *In re Longi*, 759 F. 2d 887, 897 (Fed. Cir. 1985) ("Only a reasonable expectation of success, not absolute predictability, is necessary for a conclusion of obviousness"). Put simply, the 1:1 DHP stoichiometry adds nothing to distinguish claims 1 and 2 of the '708 patent. That reality simply met what was expected does not allow Merck to extend its monopoly.

B. Claims 1 and 2 of the '708 Patent Are Not Patentably Distinct in View of the Knowledge of the POSA.

Even if one were to somehow ignore the definition of "pharmaceutically acceptable salts" in the reference '871 patent, the result would be the same because the prior art would have led a POSA to make sitagliptin DHP with a reasonable expectation of success as well. This analysis provides an independent basis that claims 1 and 2 of the '708 patent are not patentably distinct.

[5] There is no dispute that the claimed DHP salt is in fact "a pharmaceutically acceptable salt." *See* Tr. 309:19-21 (Buckton); Tr. 949:10-12 (Myerson).

As the Federal Circuit already recognized, active drug molecules are frequently made into pharmaceutically acceptable salts to improve their bioavailability. *Pfizer*, 480 F.3d at 1353; DTX-5.1; Tr. 287:8-288:2 (Buckton). In the case of a basic active drug molecule like sitagliptin, an acid is chosen to dissolve in solution with the molecule to form the salt. Tr. 288:3-12 (Buckton). Selecting the appropriate acids to dissolve with the base is a routine step in the salt selection process. *E.g.*, Tr. 282:6-284:5, 293:20-24 (Buckton). There, the POSA first determines (with ease) the pKa of the molecule. DTX-5.1; DTX-235.8; Tr. 284:13-285:25, 286:4-287:4 (Buckton). If the pKa value is different between the acid and molecule to a "suitable degree," that is, 2-3 pKa values, a salt is expected to form. DTX-5.1-2; DTX-22.3; Tr. 288:3-289:5 (Buckton). When the difference in pKa values is 3 or more, one would have "a very high expectation that you're going to form a salt." Tr. 289:20-290:4 (Buckton). What is more, the POSA does not test a single acid at a time, but rather would use what is called a "salt screen," where multiple acids (typically around 8-10 acids) are tested with the basic molecule. Tr. 293:14-19 (Buckton); Tr. 951:11-15 (Myerson); Tr. 713:16-24, 715:25-716:8 (Vydra). This salt screen is an initial, routine step in pharmaceutical development when a compound is selected to move forward into the preformulation stage. Tr. 293:20-24 (Buckton); Tr. 950:13-951:1 (Myerson).

A POSA would have been motivated to select phosphoric acid as a candidate for salt formation with sitagliptin and include it in the salt screen based on the available prior art. For example, Bastin showed that phosphoric acid was a "common pharmaceutical salt[]." DTX-5.2; Tr. 294:3-295:5 (Buckton). As another example, Bighley taught that phosphoric acid salts were among the top ten salt forms in use as of the publication date. DTX-7.4 (showing 2.48 percent of salt forms as phosphate salts, which equates to approximately 35 marketed products); Tr. 295:11-18. Bighley additionally taught a "thought process" whereby suitable salts are chosen and

produced in an efficient and timely manner. DTX-7.30-31, 35; Tr. 297:23-298:21 (Buckton). This process involves the preparation of HCl salts, and the very next consideration is mineral acid salts (such as phosphoric acid).[6] *Id.*; *see infra* Section II.E. Not surprisingly, the inventors followed the POSA's path, conducting multiple screens using phosphoric acid among numerous other acids tested. DTX-242.1-3; Tr. 155:1-156:5 (Hansen); Tr. 713:16-714:1, 715:25-716:8 (Vydra).

Further, the POSA would reasonably expect the 1:1 DHP salt to form based on the pKa of sitagliptin and pKa of phosphoric acid. Tr. 314:16-315:11 (Buckton). First, the POSA would have started the salt selection process with equimolar (same) amounts of sitagliptin to phosphoric acid. DTX-5.2; Tr. 156:6-10, 159:9-12 (Hansen); Tr. 301:23-303:1 (Buckton); Tr. 716:25-717:24 (Vydra); *see* Tr. 952:12-20 (Myerson). The pKa of sitagliptin is 7.7 and the pKa of the first proton on phosphoric acid is 1.96. Given that difference is more than three, the POSA would reasonably expect the DHP salt to form. DTX-4.1 (listing the pKa of sitagliptin as 7.7)[7]; DTX-21.182 (listing the pKa values of the three protons on phosphoric acid as 1.96, 7.12, and 12.32); Tr. 314:16-315:11 (Buckton) ("The difference is way more than three . . . you're going to predict that's going to form a salt.") (Buckton); Tr. 955:10-18 (Myerson). Though it is possible that other remote stoichiometries could theoretically have been formed because phosphoric acid has three protons that could be donated, all experts agreed that the 1:1 DHP salt would be expected to form, *i.e.*, where only the first proton is transferred from phosphoric acid. Tr. 314:16-315:11 (Buckton); *see*

[6] Plaintiffs contend that a POSA would test for an HCl salt and only consider others if that test were to fail. Tr. 860:6-11 (Myerson). That is wrong as Dr. Buckton explained (Tr. 297:23-298:21, 300:18-301:22) and as noted in *Pfizer*. *Pfizer*, 480 F.3d at 1362-63, 1367-68.

[7] While not prior art, the product information for Australian Janumet (DTX-4) lists the pKa of sitagliptin. At trial, Merck repeatedly noted that the pKa of sitagliptin was not known as of the priority date and, therefore, a POSA would not be able to conduct a pKa analysis. That is incorrect. In an OTDP analysis, the POSA starts with reference claim 17, which discloses sitagliptin. Measuring pKa is a simple, routine, and quick step conducted immediately after identifying a new chemical compound. DTX-235.8; DTX-5.1; Tr. 284:13-285:25; 286:12-287:4 (Buckton); *see* 956:7-12 (Myerson). There is no dispute that sitagliptin is a weak base. *See* Tr. 956:13-14 (Myerson).

Tr. 952:21-953:13, 954:12-955:18 (Myerson). That is because the pKa values for the second and third protons of the phosphoric acid are too close to the pKa value of sitagliptin or above that value. Tr. 314:16-315:11 (Buckton); *see* Tr. 955:14-18 (Myerson). Therefore, the remote possibility that salts other than the DHP salt *might* form does not negate that the DHP salt *would* be the one a POSA would reasonably expect. Tr. 314:16-315:11 (Buckton). Again, mere possibility does not trump what is expected. And, Dr. Buckton's opinion is ultimately confirmed by the book of wisdom where a Merck scientist, a lab tech with a skill level below the defined POSA, created the DHP salt on her first try with a basic salt screen. Tr. 727:16-729:2 (Vydra). In addition, Dr. Hansen, another inventor that did hundreds of reactions with sitagliptin and phosphoric acid, never created anything other than the 1:1 DHP salt. Tr. 159:13-18, 162:6-9, 162:22-163:1, 163:8-11, 163:19-22 (Hansen). For these additional reasons, claims 1 and 2 of the '708 are not patentably distinct even if one were to simply ignore the express teachings of the reference '871 patent.

C. Claim 3 of the '708 Patent Is Not Patentably Distinct in View of the Knowledge of the POSA.

Claim 3 of the '708 patent depends from claim 1, and differs only in that the claimed compound be in the (S)-configuration. Ex. A at 3; Tr. 281:2-6; 316:21-317:2 (Buckton). Claiming the (S)-configuration separately does not alter the OTDP analysis. The (R)- and (S)- are the **only** two possible stereoisomers for sitagliptin because there is only one chiral center in that compound. Tr. 316:21-317:13 (Buckton); Tr. 957:25-958:11 (Myerson); JSOF ¶ 121. If there is only one chiral center, when one knows the (R), one knows the (S). Tr. 317:8-13 (Buckton). And as far as a reasonable expectation of success in making the (S)-, if the (R)- is known, then the POSA could make the (S)- with ease. Tr. 318:9-13 (Buckton); Tr. 958:7-22, 959:5-8 (Myerson).

Lastly, a POSA would also have been motivated to develop the (S)-configuration because different configurations can have different biological properties. Tr. 317:14-16 (Buckton).

Because of the potential for isomers to have differing properties, the FDA required studying chiral centers to determine their activity. Tr. 317:17-20 (Buckton). Specifically, FDA's prior art Policy Statement for the Development of New Stereoisomeric Drugs states "[t]he stereoisomeric composition of a drug with a chiral center should be known and the quantitative isomeric composition of the material used in pharmacologic, toxicologic, and clinical studies known." DTX-48.2. The POSA is "obliged to look at the two isomers."[8] Tr. 317:21-318:8 (Buckton). For these reasons, a specific claim to the (S)-configuration of sitagliptin can no more withstand OTDP scrutiny than aforementioned claims 1 and 2 of the '708 above.

D. Claim 19 of the '708 Patent Is Not Patentably Distinct.

Reference claim 20 of the '871 patent covers "[a] pharmaceutical composition which comprises an inert carrier and a compound of claim [17]." DTX-2054.22 at 41:21-22, 23.[9] The '871 patent further describes the use of such compositions in the treatment of type II diabetes. Claim 19 of the '708 patent covers a "method for the treatment of type 2 diabetes comprising administering to a patient in need of such treatment a therapeutically effective amount of the salt according to claim 2." JTX-1.15 at 17:29-32; Tr. 281:6-13 (Buckton).[10] A method of treatment claim like this one does not survive OTDP when it merely covers "a particular use" of a compound or composition and that "particular use" is described in the reference patent. *E.g., Pfizer v. Teva*, 518 F.3d 1353, 1363 (Fed. Cir. 2008) ("Thus, we agree with the district court that the '068 patent merely claims a particular use described in the '165 patent of the claimed compositions of the '165 patent" and therefore does not survive OTDP); *see also Geneva Pharm.*, 349 F.3d at 1385-86.

[8] Both before and during trial, Plaintiffs have raised the IPR. On that point, the PTAB did not consider the FDA's Policy Statement during the IPR, nor did it consider OTDP of any claim.
[9] As originally written, reference claim 20 depended from claim 16. It was subsequently corrected to depend from claim 17. DTX-2054.23; Tr. 318:20-25 (Buckton).
[10] As an initial matter, because reference claim 20 depends from reference claim 17, the analysis in Sections II.A and B are incorporated herein.

Claim 19 of the '708 patent does nothing more than claim a described use (treating type II diabetes) for the sitagliptin DHP salt (or hydrates thereof) of claim 2. But, the reference '871 patent is clear: the claimed compounds (which include sitagliptin and its pharmaceutically acceptable salts) "have utility in the treatment of type II diabetes." DTX-2054.6 at 9:34-35; DTX-2054.1 at Abstract; Tr. 309:5-12, 311:11-15 (Buckton); *see AbbVie*, 764 F.3d at 1380-81 (looking "to a reference patent's disclosures of utility to determine the question of obviousness"). Merck may argue that the utility statements in the '871 reference patent apply generically to hundreds of compounds, and therefore a POSA would not know that sitagliptin in particular would be therapeutically effective for treating type II diabetes. But that is not true. The reference '871 patent contains a total of 26 claims, only *two* of which are independent claims directed to single, specific compounds (including reference claim 17). DTX-2054.18-22 (claims 1-26). Two more are dependent claims to pharmaceutical compositions of those specific compounds (including reference claim 20). The remainder of the claims are directed to large genera of compounds. DTX-2054.18-22. Since only two pharmaceutical compositions were claimed, one being directed to sitagliptin or a pharmaceutically acceptable salt thereof, a POSA would readily understand that the utility disclosures apply to sitagliptin. DTX-2054.6 at 9:34-35; Tr. 957:22-24 (Myerson).[11]

A POSA would also understand that the purpose of the "pharmaceutical composition" of reference claim 20 is to deliver a "therapeutically effective amount" to a patient in need. Tr. 320:5-14 (Buckton). After all, treating a patient effectively is the "ultimate goal of a pharmaceutical composition." *Id.* Further, Merck specifically defined the term "composition" as used in reference claim 20 to be one made by "admixing a compound of the present invention and a pharmaceutically

[11] Merck may also argue that the '871 patent discloses more than one utility, not just the treatment of type II diabetes. But even if true, it is completely irrelevant to the OTDP analysis. *See Sun*, 611 F.3d at 1386 ("the analysis in the *Pfizer* decision shows that [OTDP] encompasses *any use* for a compound that is disclosed in the specification of an earlier patent claiming the compound.") (emphasis added).

acceptable carrier. By 'pharmaceutically acceptable' it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious ***to the recipient thereof***." DTX-2054.5 at 8:14-33 (emphasis added); Tr. 319:4-22 (Buckton). Thus, the POSA would be motivated to provide the compound of reference claim 20 to *recipients* for the treatment of type II diabetes. This is precisely the situation that caused the Federal Circuit to reject the asserted claims in *Pfizer v. Teva*. 518 F.3d at 1363 ("The claims at issue of the '068 patent merely recite methods of administering a 'therapeutically-effective amount' of the compositions found in claim 5 of the '165 patent.").

That alone ends the inquiry. But based on reference claim 20 and the utility and claim boundaries described in the '871 specification, the POSA would also have a reasonable expectation of success in determining the "therapeutically effective amount"[12] as covered in claim 19 of the '708 patent. First, Merck does not dispute that sitagliptin is "an orally **active** inhibitor of the dipeptidyl peptidase (DPP-4) enzyme." JSOF ¶ 6 (emphasis added). Second, the '871 patent discloses specific dosage amounts for sitagliptin and, in particular, that the dosage amounts for humans will generally be from about 7 mg to 350 mg daily. DTX-2054.9 at 16:51-54; Tr. 320:15-321:4 (Buckton). This dosage amount *does not vary* depending on the free base or salt form used; once dissolved in a patient, any crystalline form will no longer be crystalline and any salt will no longer be a salt. Tr. 321:5-322:4. It is the "active moiety," which is the molecule that provides any therapeutic effect in the patient's system. *Id.*; JSOF ¶ 6. That is why the '708 patent (directed to the salt) is no different from the '871 patent utility disclosure (directed to sitagliptin). Indeed, the '708 patent specification gives all of this short shrift, "[a]n ordinarily skilled physician,

[12] There is no amount specified in claim 19 of the '708 patent. The claim states a "therapeutically effective amount" without more. JTX-1.15 at 17:29-32. Merck cannot argue that a POSA could not determine the therapeutically effective amount of sitagliptin when the '871 patent claims a "therapeutically effective amount" of an entire genus of compounds for the same disease. *See* DTX-2054.22 at 42:5-9 (claim 23).

veterinarian, or clinician can readily determine and prescribe the effective amount of the drug required to prevent, counter or arrest the progress of the condition." JTX-1.9 at 5:31-34; Tr. 321:5-322:4 (Buckton).

Now, Merck proffered the testimony of its longtime consultant and publicly acknowledged collaborator,[13] Dr. MacMillan, in an attempt to rebut this clear disclosure of utility in Merck's own '871 patent. Tr. 793:24-795:13, 796:15-22 (MacMillan). And while no one takes away from Dr. MacMillan his Nobel Prize in catalyst reactions—while at the "Merck" institute at Princeton where he remains today—he is admittedly not an expert on the issues in dispute here: he is not an expert in diabetes; he is not a physician or clinician; and he has never determined a therapeutic dose for a patient for any drug, among other things. Tr. 798:19-799:21 (MacMillan). Dr. MacMillan provided no testimony that sitagliptin DHP had any difference in clinical efficacy compared to sitagliptin free base or another pharmaceutically acceptable salt as claimed in the '871. That latter omission is not surprising as, like the '871 patent, the '708 patent does not disclose any clinical data. Tr. 805:7-9 (MacMillan). Thus, both patents—devoid of clinical data—simply provide for the same effective treatment of type II diabetes, while disclosing ranges of therapeutically effective amounts. In that circumstance, Federal Circuit precedent is clear that one cannot extend patent life simply by claiming that a compound can be used in a therapeutically effective amount to treat the same disease disclosed in the reference patent. *See Pfizer v. Teva*, 518 F.3d at 1363.

E. Claims 1-3 and 19 of the '708 Patent Are Not Patentably Distinct in View of WO'498 or Bighley.

Finally, at trial, two additional combinations were presented by Mylan that provide a third reason that the asserted claims of the '708 patent cannot survive the OTDP analysis. Specifically,

[13] It is respectfully noted that Dr. MacMillan's long-time collaboration with Merck does inform on his objectivity here. Perhaps Merck posits it best when it states that Dr. MacMillan "has been a very strong advocate for Merck chemistry throughout his career." Tr. 795:4-13 (MacMillan).

both Bighley (DTX-7) and WO '498[14] (DTX-36) additionally support the arguments discussed in Sections II.A-D (which are incorporated herein). Bighley teaches that "[s]alt formation is frequently performed on weak acidic or basic drugs because it is a relatively simple chemical manipulation which may alter the physicochemical, formulation, biopharmaceutical, and therapeutic properties of a drug without modifying the basic chemical structure." DTX-7.3; Tr. 325:5-18 (Buckton). And as discussed above, phosphoric acid was one of the most commonly used acids in salt formation according to Bighley (DTX-7.4; Tr. 295:23-297:22 (Buckton)) and would have been included in a sitagliptin salt screen. *Supra* Section II.B; DTX-5.2; DTX-7.30-31, 35; Tr. 294:3-295:5, 295:11-18, Tr. 297:23-298:21 (Buckton); *see Pfizer*, 480 F.3d at 1363-65.

As to WO '498, if one were to ignore the specification of the '871 patent as Merck seeks to do, WO '498[15] discloses the same information because it shares the same specification describing eight "particularly preferred" acids, including phosphoric acid. DTX-36.11 at 14-15; Tr. 327:8-24 (Buckton). With respect to the 1:1 stoichiometry, Example 7 of WO '498 teaches that when an *excess* amount of HCl is used in a reaction with sitagliptin free base—that is, when more than one HCl molecule is available to react with each molecule of sitagliptin—only a 1:1 sitagliptin salt forms. DTX-36.47; Tr. 328:7-22 (Buckton). Given that HCl (pKa of -6), a much stronger acid than phosphoric acid, only resulted in a single proton transfer, it suggests to a POSA that using phosphoric acid would also result in the 1:1 DHP salt (single proton transfer). DTX-21.214; Tr. 328:7-22 (Buckton). With respect to claim 3 of the '708 patent, WO '498 specifically

[14] Merck contends that WO '498 cannot serve as prior art to the '708 patent in an OTDP analysis pursuant to 35 U.S.C. § 103(c). This was squarely addressed in *Germeyer*, where the court held that to the extent § 103(c) prevents the use of art that qualifies as prior art only under one or more of subsections (e), (f), and (g) of § 102, § 103(c) ***does not*** apply to an OTDP analysis. *Ex Parte Germeyer*, No. 2009-010346, 2010 WL 1253701, at *5 (B.P.A.I. Mar. 29, 2010).

[15] The specifications of the '871 patent and WO '498 are identical. Thus, in the above OTDP analyses, the references to the specification of the '871 patent are interchangeable with references to WO'498. Tr. 327:25-328:6 (Buckton). For brevity, Mylan does not repeat those arguments.

discloses both the (R)- and (S)-configuration of sitagliptin. *See* DTX-36.9 at 19-28; Tr. 329:1-13 (Buckton). WO '498 discloses that "[e]ach such asymmetric [chiral] center will independently produce two optical isomers . . . . The present invention is meant to comprehend all such isomeric forms of these compounds." DTX-36.9 at 24-28. Lastly, with respect to claim 19 of the '708 patent, WO '498 discloses specific dosage amounts for humans from about 7 mg to 350 mg daily. DTX-36.25 at 3-5. Thus, WO '498 also provides motivation and expectation of success in developing the subject matter of the asserted claims.

F. Merck Failed to Rebut the Strong *Prima Facie* Case of Invalidity.

Merck's purported evidence on secondary considerations does not overcome the strong showing that the asserted claims of the '708 patent are *prima facie* invalid. *See Pfizer*, 480 F.3d at 1372. Regardless though, to show unexpected results, Merck needed to tell the Court what one would expect from the DHP salt of sitagliptin. Merck did not. One cannot find an unexpected result when one failed (as Merck did here) to establish what the expected result would be. *Pfizer*, 480 F.3d at 1371 ("Thus, in order to properly evaluate whether a superior property was unexpected, the court should have considered what properties were expected.").

Merck also did not raise any secondary considerations of non-obviousness with respect to asserted claims 3 and 19. *See* Tr. 983:7-10 (Buckton); Tr. 960:18-24, 961:3-13 (Myerson). With respect to claims 1 and 2, however, Merck failed for additional reasons. First, Merck failed to support unexpectedly superior properties for the full scope of claims 1 and 2. Notably, Merck abandoned anhydrous Forms I-III of sitagliptin DHP due to stability and processability issues and Forms I-III fall within the scope of the asserted claims. DTX-283.45; Tr. 981:4-13, 983:3-6 (Buckton).[16] And even assuming, *arguendo*, the monohydrate form used in Merck's Januvia and

[16] Mylan's ability to stabilize Form I does not undermine that Merck had stability issues with Forms I-III and was unable to stabilize Form I. Tr. 694:25-697:13 (Cockcroft); DTX-2102.14-15; DTX-2092.3-43.

Janumet products (*see* JSOF ¶ 7) has unexpected properties (which it does not), the monohydrate is covered by dropped claims 4-16 and therefore cannot support unexpected results for the full scope of far broader claims 1 and 2. Thus, Merck failed to meet its burden to show unexpected results commensurate in scope with the asserted claims. *See* Tr. 983:3-6 (Buckton); *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 965 (Fed. Cir. 2014) (unexpected results must be "commensurate with the scope of the claims.").[17]

Merck points to supposed unexpectedly superior properties for the DHP salt with respect to morphology, hygroscopicity, chemical stability, or thermal stability. But as the trial record makes clear, the very reason POSAs develop salts of compounds is to improve these types of properties for the ultimate goal of creating a suitable pharmaceutical composition. Tr. 983:15-984:9 (Buckton). Telling is Merck's later filed WO '530 patent application, which boasts that the same or similar properties *of other sitagliptin salts* are advantageous for the preparation of pharmaceutical compositions. DTX-282.3 at 10-21; Tr. 986:17-23 (Buckton). When other salts have the same properties, those properties are not unexpected. *Pfizer*, 480 F.3d at 1371 ("The district court wrongly relied on the fact that the 'besylate salt works' because considerable evidence shows that amlodipine maleate also worked for its intended purpose . . ."). Finally, non-DHP salts were approved and sold in countries outside the U.S., further indicating that any alleged unexpected superiority is that of degree and not kind. Tr. 993:23-994:5 (Buckton). Merck's lone secondary consideration does not save the claims.

III. THE ASSERTED CLAIMS OF THE '708 PATENT ARE INVALID UNDER § 112.

Claims 1, 2, 3, and 19 also fail under § 112. According to Merck, these claims cover all hydrates, whether in Merck's possession or not. Tr. 913:2-9 (Myerson); Tr. 980:19-24 (Buckton);

[17] Similar to its failures with claim 3, Merck failed to offer any secondary considerations of non-obviousness concerning sitagliptin in the (S)-configuration covered by claim 1.

D.I. 91-2 at p. 46 (listing common hydrates). Merck admits it took this aggressive position in claim construction (at least as to claims 2 and 3) to save the monohydrate claims. Tr. 34:24-35:2. Having prevailed on its claim construction, Merck must now show how its construction survives § 112 scrutiny: "[I]f [Merck] want[s] to exclude others from what it regard[s] as its invention, its patent need[s] to teach the public how to make and use that invention. That is part of the *quid pro quo* of the patent bargain … to some extent, [Merck] created its own enablement problem." *Trustees of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1365 (Fed. Cir. 2018).[18] As was evident at trial, the full scope of the claims cover all hydrates, anhydrous forms, and amorphous forms. Tr. 336:13-20 (Buckton); Tr. 941:4-7, 961:14-21 (Myerson). But Merck only enabled a single hydrate, a monohydrate, and a dehydrated form of that single hydrate. Tr. 334:9-12 (Buckton); Tr. 937:14-18 (Myerson). That is not sufficient to meet the § 112 requirements.

A. Enablement.

To be enabling, the specification "must teach those skilled in the art how to make and use the **full scope of the claimed invention** without undue experimentation." *Bos. Univ.*, 896 F.3d at 1362 (citations and quotations omitted) (emphasis added). Even if a patent enables five out of six permutations within the scope of the patent, that is still not good enough; the specification must enable everything claimed. *See id*. at 1364. (holding a patent invalid under this scenario). "[A] patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012).

True, the specification need not "expressly spell out every possible iteration of every claim" because those gaps can be filled with "the artisan's knowledge of the prior art and routine

[18] All of the asserted claims suffer from the same deficiencies, and thus, are invalid for the same reasons as each individual claim. Tr. 335:23-336:7 (Buckton); 932:19-23, 961:14-17 (Myerson).

experimentation." *Bos. Univ.*, 896 F.3d at 1364; *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). But that does not help Merck here. Its expert testified that no forms of sitagliptin DHP were known publicly before the filing date of the '708 patent. Tr. 921:13-16, 935:19-23 (Myerson); SOF at ¶ 72. Merck told the PTAB the same thing.[19] IPR2020-0040, Ex. 2101, Myerson Declaration, at ¶ 148. So, no prior art could fill the gaps. And as outlined below, undue experimentation (*i.e.*, not routine experimentation) would be necessary to fill the gaps. As such, Merck has violated the enablement requirement.

1. Merck is Not Entitled to More Than What it Actually Discovered.

The parties agree that Merck discovered and possessed the particular monohydrate recited in claims 4-16 of the '708 patent. Though Merck contended that Mylan infringed those claims up to the eve of trial, those claims were rightfully dropped and will survive regardless of the outcome of this case. D.I. 143. The question here, therefore, is whether Merck is entitled to monopolize *more* than what it actually discovered, possessed, or taught how to make—*i.e.*, all hydrates. The answer is no. Section 112 prohibits such a perverse outcome. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1321 (Fed. Cir. 2005) ("The patent system is based on the proposition that the claims cover **only** the invented subject matter.").

Both parties' experts agree that "it always is possible to find additional crystalline forms," which would include other hydrates and anhydrous forms. Tr. 919:10-11 (Myerson); Tr. 937:2-4 (Myerson); Tr. 338:11-20 (Buckton). "[T]he literature abounds with new polymorphic forms being found or created years or decades after a molecule was first synthesized[.]" Tr. 937:10-13 (Myerson); DTX 2141.44. In fact, "we know that [polymorphism] will probably happen, but not

[19] *Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp.*, IPR2020-00040 (P.T.A.B.). The IPR proceedings are considered a part of the intrinsic record of the patent. *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360-61 (Fed. Cir. 2017).

why or *when*." PTX-282.16 (emphasis added); *see also* Tr. 947:23-948:5 (Myerson); PTX-213 at 2 ("[A]nd the number of polymorphs of a material depends on the amount of time and money spent in research on that compound."). But enablement does not hinge on whether the claimed invention is *possible* to create.

It is about whether the specification *as written* tells a person skilled in the art how to make and use it without undue experimentation. *Amgen Inc. v. Sanofi*, 987 F.3d 1080, 1084 (Fed. Cir. 2021). As the Federal Circuit recently put it, "the law is clear that a patent cannot be awarded for mere theoretical research without more." *Biogen Int'l GMBH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1344 (Fed. Cir. 2021). "Tossing out the mere germ of an idea does not constitute enabling disclosure." *In re '318 Pat. Infringement Litig.*, 583 F.3d 1317, 1324 (Fed. Cir. 2009) (internal quotations and citations omitted)). Yet that is all Merck did. It cannot support a claim to all hydrates on this record by describing one monohydrate embodiment. *LizardTech, Inc. v. Earth Resource Mapping, Inc.* is illustrative. 424 F.3d 1336, 1346 (Fed. Cir. 2005). "To hold otherwise would violate the Supreme Court's directive that '[i]t seems to us that nothing can be more just and fair, both to the patentee and the public, than that the former should understand, and correctly describe, just what he has invented, and for what he claims a patent." *Id.* (*citing Merrill v. Yeomans*, 94 U.S. 568, 573-574 (1876)).

2. The *Wands* Factors Support a Finding of Non-Enablement.

Though enablement is not precluded by the necessity of some experimentation, that experimentation cannot be undue. In *In re Wands*, the Federal Circuit set forth factors when determining if a disclosure requires undue experimentation.[20] 858 F.2d 731, 737 (Fed. Cir.

[20] These factors include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the relative skill of those in the art, (5) the nature of the invention, (6) the state of the prior art, (7) the predictability or unpredictability of

1988).[21] On this record, the *Wands* factors support the conclusion that the asserted claims are not enabled because undue experimentation would be required to practice the full scope of the claims.

a. Breadth of the claims

Merck fought—and won—a broad claim construction that encompasses *any hydrate*. Dr. Myerson repeatedly testified on behalf of Merck that the scope of the asserted claims cover the 1:1 DHP salt in *any physical form*, including hydrates. (Myerson testifying that asserted claims cover: (i) both stoichiometric and unstoichiometric hydrates (Tr. 934:2-5; 935:6-8); (ii) all anhydrous forms (Tr. 937:19-22); (iii) all noncrystalline forms and crystalline forms (Tr. 939:18-25)). There is no dispute between the parties or their experts on this point. Tr. 336:16-20 (Buckton) (same).

But when it came time for Dr. Myerson to fit the asserted claims within the first *Wands* factor, he made an about face. Asked whether the phrase "or a hydrate thereof" in claim 1 of the '708 patent renders it a broad claim, Dr. Myerson responded: "No. Because there's only one" hydrate of the 1:1 DHP salt. Tr. 923:16-18 (Myerson); *see also* Tr. 934:22-24 (Myerson) (monohydrate encompassed in the term hydrate); Tr. 935:9-12 (Myerson) (monohydrate form only one of the seven common hydrates). But if another hydrate were found by anybody else, Dr. Myerson asserted that Merck would own it. Tr. 948:7-10 (Myerson). Dr. Myerson's irreconcilable testimony underscores the terminal defect in Merck's argument. It intentionally pursued claims that were broader than what it had at the time of filing and what it described to the public. Again, Merck's claims on the specific monohydrate that it discovered and possessed are unchallenged and will survive this case. *Phillips*, 415 F.3d at 1321. But Merck is not entitled to *more*.

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the art, and (8) the breadth of the claims. 858 F.2d 731, 737 (Fed. Cir. 1988). The relative skill of those in the art is a neutral factor, and thus, Mylan does not address it herein.

[21] A court need not consider every one of the *Wands* factors in its analysis, only those relevant to the facts of the case. *See, e.g., Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999).

Again, Merck attempts to undercut this through Dr. Myerson's testimony that the claim is narrow because it is to a particular salt. Tr. 923:2-11 (Myerson). In so doing, Merck ignores its prior claim construction position. It is not a particular salt, or compound, that is claimed—as Merck has made clear, it is that salt in any physical form (including all hydrates). Tr. 913:2-9 (Myerson). The "any physical form" is the issue, which expands the breadth of the claim, because as Dr. Myerson conceded on cross-examination, the compound by itself does not provide all polymorphic forms of that compound. Tr. 945:1-5, 945:8-13 (Myerson). These are broad claims, and this *Wands* factor weighs in favor of undue experimentation.

b. The quantity of experimentation necessary, the amount of direction or guidance presented, and the presence or absence of working examples

Skilled artisans hoping to obtain the results under Merck's broad claims would find themselves adrift. As to the amount of experimentation necessary, there would be a virtually infinite amount of work due to the unpredictability of polymorphism and hydrate formation. Tr. 339:1-24 (Buckton); PTX 213.0002; Tr. 938:8-13 (Myerson). At trial, Dr. Myerson refused to provide an opinion on whether finding another hydrate would require undue experimentation. Tr. 936:18-23, 936:7-10 (Myerson); Tr. 340:3-15 (Buckton). But on behalf of Merck in the IPR, Dr. Myerson was more forthcoming, and his statements apply here: "It is therefore my opinion that the prior art would not have enabled the POSA to make a crystalline monohydrate form of sitagliptin [DHP] without undue experimentation." IPR2020-0040, Ex. 2101 at ¶ 184; *id*. at ¶ 63; *id*. ("The unpredictability of crystalline forms applies equally in the context of solvates and hydrates.").

Further, it is undisputed that the '708 patent does not contain any working examples of any hydrates other than a single monohydrate and its unstable dehydrated form. Tr. 342:20-343:5 (Buckton); Tr. 925:10-13,941:1-3 (Myerson); Tr. 971:15-18 (Myerson) ("example for making the

one crystalline monohydrate"); Tr. 165:3-9 (Hansen). Nor does the '708 patent provide any guidance to synthesize or characterize any hydrates beyond the method for the single disclosed monohydrate. Tr. 339:6-9 (Buckton). Accordingly, these factors favor undue experimentation.

c. The nature of the invention and the state of the prior art

As the Claim Construction Order explains, the nature of the invention of the asserted claims is very broad, and includes multiple forms of sitagliptin DHP, including hydrates. D.I. 93-20 at 12; 343:11-16 (Buckton). Again, this is consistent with Dr. Myerson's opinions that the asserted claims cover sitagliptin DHP in any state of matter, and his sworn statements during claim construction. D.I. 91-2 at ¶¶ 56, 61; Tr. 933:12-20 (Myerson); JSOF at ¶ 50. This is so regardless of Dr. Myerson's theory that the nature of the invention is the salt itself. Tr. 925:23-926:1 (Myerson). Were it that, the specification and (now) unasserted claims would not have been devoted almost exclusively to the crystalline monohydrate. Indeed, immediately preceding that line of questioning at trial, Dr. Myerson testified that the nature of the invention is not just the salt itself, but that salt in "all of its physical forms." Tr. 925:21-22 (Myerson). Given the all-encompassing nature of the purported invention, undue experimentation would be required.

As to the state of the prior art, Dr. Myerson takes the strained position that a POSA reading the '708 patent would know how to prepare various forms of sitagliptin DHP and that the prior art disclosed general characterization methods. Tr. 926:6-11 (Myerson). This testimony cannot be reconciled with Merck's and Dr. Myerson's previous statements in the IPR when defending the validity of the no longer asserted monohydrate claims. Tr. 343:20-25 (Buckton quoting Myerson Report) ("the prior art provided no guidance whatsoever . . . about what conditions might be appropriate for synthesizing any hydrate, much less the crystalline monohydrate of Claim 4."); *see also* IPR2020-0040, Paper 41, at 52. Without prior art providing any guidance on sitagliptin salts

forming hydrates and the unpredictability of crystalline forms generally (more on that below), the POSA would need to undertake undue experimentation. Tr. 935:25-936:3 (Myerson).

d. The predictability or unpredictability of the art

Lastly, Merck cannot dispute that the formation of new solid forms is highly unpredictable. Tr. 344:18-22 (Buckton); Tr. 927:16-22 (Myerson); IPR2020-0040, Ex. 2101 at ¶¶ 58, 60, 63, 69, 79. Dr. Myerson himself provides the majority of the proof on this issue through his opinions and supporting materials on unpredictability of the art. Tr. 939:10-19 (Myerson) (relying on PTX-93 at 1); Tr. 942:3-14 (Myerson); PTX-91 ("Tales of difficulties in obtaining crystals of a particular known form or in reproducing results from another laboratory, or even from one's own, abound. Indeed, there are cases where it was difficult to obtain a given polymorphic form, even though this had previously been obtained routinely over long time periods.") (emphasis added)); Tr. 943:17-23, 945:1-7 (Myerson); DTX-47.16 ("Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds."); *see also* IPR2020-00040, Ex. 2101 at ¶¶ 60-63. Merck readily concedes and has repeatedly argued that the art is unpredictable; undue experimentation would be required.

3. Merck's Statements Regarding Forms I-III Cannot Be Reconciled.

Nowhere is Merck's overreach more evident than its allegation that claims 1-3 and 19 also cover anhydrous forms, which were specifically disclosed and claimed in a separate patent application that Merck chose to abandon and deliberately exclude from the '708 patent disclosure. JSOF at ¶¶ 64-66, 69, 71, 72; Tr. 940:15-17, 961:22-962:4 (Myerson). On one hand, Merck contends that the claims are enabled because the patent discloses the only hydrate known at the time. 915:25-916:3 (Myerson). On the other hand, Merck knew of anhydrous Forms I-III prior to filing the '708 patent application (JSOF at ¶ 72), even though the '708 patent does not enable Forms I-III. These forms are not described or even referenced in the specification of the '708

patent. Tr. 937:23-25 (Myerson); Tr. 341:9-17 (Buckton). Rather, Merck fully described and specifically claimed those forms in a separate and unrelated patent application, which it later abandoned. JSOF at ¶¶ 64-66, 69, 71, 72; Tr. 940:15-17, 961:22-962:4 (Myerson). Perhaps in an effort to rectify this defect, Merck's paid fact witness (Dr. Hansen) as well as Dr. Myerson to put forth arguments that the specification of the '708 patent suggested or taught a POSA how to make anhydrous Forms I-III. Tr. 140:9-15 (Hansen); Tr. 918:7-23 (Myerson).

But Merck's position before this Court is the exact opposite of what it took before the Patent Office during prosecution of the '708 patent. Specifically, in an effort to distinguish the '708 patent application from their application to these anhydrous forms, the patentees (including Dr. Hansen, a named inventor on both applications) were unequivocal: "[t]he Applicants maintain that dihydrogenphosphate salt and the crystalline monohydrate form of the ['708] application do not suggest the crystalline anhydrate pseudopolymorph of copending Application No. 10/569,566." JTX-4.250. Dr. Myerson conceded this on cross-examination. Tr. 969:20-970:19 (Myerson). Merck cannot rescue the '708 patent by retreating from the intrinsic record.

B. Written Description.

Whether written description is satisfied is a question of fact. *Biogen*, 18 F.4th at 1340-41. That requirement demands "possession as shown in the disclosure." *Ariad Pharms.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). Both experts testified that a POSA reviewing the '708 patent would recognize that the inventors did *not* have possession of any other hydrate of the DHP salt other than the *single* disclosed (monohydrate) species. Tr. 937:14-18 (Myerson); 334:9-12 (Buckton).

Merck relies on *GlaxoSmithKline*, but that case supports Mylan. 744 F.3d 725 (Fed. Cir. 2014). There, the Court's holding rested on the known susceptibility of the specific active pharmaceutical ingredient (dutasteride) for solvate formation. *Id*. at 731 ("[s]teroids in particular [such as dutasteride] have been known to be prone to solvate formation since 1983"); *id*. at 728

(district court "found that dutasteride is 'the key structural feature of the solvate' and what 'distinguish[es] the '467 patent from the prior art.'") (alterations in originals). Both sides agree that sitagliptin was not known to be susceptible to hydrate formation. Tr. 952:5-10 (Myerson); Tr. 421:18-20 (Buckton). Dr. Myerson went even further and testified that not all compounds can form hydrates and that "generalizations cannot be made for a series of related compounds" as "[e]ach solid compound responds uniquely to the possible formation of solvates or hydrates." Tr. 943:21-23, 944:8-11, 939:23-25 and 944:13-18 (Myerson); DTX-47.0016. The facts of this case swing away from *GlaxoSmithKline* and in favor of invalidity for lack of written description.

GlaxoSmithKline also expressed concern with a patent that "attempt[s] to preempt the future before it has arrived." 744 F.3d at 731. But, the '708 patent does exactly that. Even though the experts agree that Merck was only in possession of one crystalline monohydrate form at the time of patent filing, the claims plainly cover all hydrates, known or unknown, at the time of filing or in the future. That is improper. The written description "requirement is satisfied only if the inventor conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and demonstrates that by disclosure in the specification of the patent." *Nuvo Pharm. (Ir.) Designated Activity Co. v. Dr. Reddy's Labs. Inc.*, 923 F.3d 1368, 1376 (Fed. Cir. 2019) (alterations and quotations omitted.) And as recently as three months ago, the Federal Circuit underscored that the "written-description requirement limits patent protection only to individuals who perform the difficult work of producing a complete and final invention featuring all its claimed limitations and publicly disclose the fruits of that effort." *Biogen*, 18 F.4th at 1344. That "difficult work of producing" other hydrates was not done here. *Id*. Merck is not entitled to claim that which it did not invent.

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CERTIFICATE OF SERVICE

I hereby certify that on this 28th day of January 2022, I filed the foregoing **"Mylan's Opening Post-Trial Brief"** with the clerk of the Court by using the CM/ECF system, which will send notification of the same to the following counsel of record:

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